

**REMARKS**

Claims 1-10 and 15-17 are pending in the application. Claims 1-7 have been amended, claims 11-14 have been canceled; and claims 15-17 have been added.

The amendments find support throughout the specification and original claims, e.g., at the paragraph bridging pages 4-5; at the paragraph bridging pages 13-14; and in Examples 1-4 on pages 16-18. No new matter has been added.

**Foreign Priority**

The Office Action acknowledges receipt of foreign priority papers submitted under 35 U.S.C. § 119(a)-(d) as well as Applicants' claim for foreign priority to JP 2003-336438, filed September 26, 2003.

In response, Applicants thank the Examiner for acknowledging receipt of the foreign priority papers, as well as Applicants' claim to foreign priority.

**Information Disclosure Statement**

The Office Action acknowledges receipt of the Information Disclosure Statements filed June 26, 2006; July 24, 2006; May 8, 2009; and June 17, 2009, as well as consideration of the documents cited therein. However, the Office Action further indicates that the Information Disclosure Statements filed July 24, 2006; May 8, 2009; and June 17, 2009 have not been considered because they were not accompanied by a Form PTO-1449.

In response, Applicants submit that an examiner may consider and indicate consideration of information that is not listed in a Form PTO-1449. Applicants further submit that an

Information Disclosure Statement need not be accompanied by a Form PTO-1449 to be compliant with 37 C.F.R. §§ 1.97 and 1.98.

Accordingly, Applicants respectfully request that the Examiner indicate consideration of the Information Disclosure Statements of July 24, 2006; May 8, 2009; and June 17, 2009.

### **Requirement for Restriction**

The Office Action makes final the Requirement for Restriction mailed October 17, 2008.

Without acquiescing to the propriety of the Requirement for Restriction, Applicants note that claims 11-14 have been canceled. Applicants further submit that cancellation of claims 11-14 is without prejudice or disclaimer, and that Applicants expressly preserve the right to prosecute the subject matter of the canceled claims in one or more divisional and/or continuation applications.

### **Claim Objections**

The Office Action objects to claims 1-7 for recitation of an acronym without a corresponding complete term, i.e., for recitation of “L-PGDS” without recitation of “lipocalin-type prostaglandin D synthase.”

In response, Applicants submit that the instant amendment is responsive to the present objections and respectfully request withdrawal of the same.

### **Claim Rejections – 35 U.S.C. § 112, First Paragraph (Enablement)**

The Office Action rejects claims 1-10 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. In particular, the Office Action states that

the claimed subject matter is enabled for a method of detecting or differentiating rheumatoid arthritis (RA), a method of determining the stage of disease with regard to RA and determining the degree of dysfunction with regard to RA wherein the levels of human L-PGDS in a sample collected from a subject without renal or heart disease or other diseases known to affect the level of L-PGDS is measured, wherein the levels of human L-PGDS measured is compared to the levels of human L-PGDS in a patient known to have RA. However, the Office Action states that the specification does not reasonably provide enablement for the instant methods of detecting or differentiating RA, a method of determining the stage of disease with regard to RA and determining the degree of dysfunction with regard to RA as claimed. In particular, the Office's position appears to be that there would be an undue amount of experimentation required to practice the invention wherein L-PGDS levels are measured in samples from patients with allegedly confounding diseases.

In response, Applicants submit that the claimed subject matter is described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected, to make and use the invention. In particular, and without acquiescing to the propriety of the rejection, Applicant's submit that claim 1 as amended is drawn to "[a] method of detecting or differentiating rheumatoid arthritis, comprising:

measuring the level of human lipocalin-type prostaglandin D synthase (L-PGDS) in a sample collected from a subject free of renal disease and/or ischemic heart disease; and

detecting or differentiating rheumatoid arthritis if the level of L-PGDS is higher in the sample collected from the subject free of renal disease and/or ischemic heart disease than it is in a healthy volunteer and/or in a patient with a joint disease other than rheumatoid arthritis." Thus,

the claimed subject matter is directed to, e.g., measurements taken from samples collected from a subject that does not have renal disease or ischemic heart disease.

Applicants further submit that one of ordinary skill in the art would know how to distinguish RA from other diseases, for example other forms of arthritis, without undue experimentation. For example, the specification discloses that L-PGDS concentrations can be measured in body fluids collected from healthy volunteers and/or patients affected with joint disease other than RA (see page 13, lines 6-18). The distributions of L-PDGS concentrations in the case of patients affected with joint diseases other than RA and/or healthy volunteers can then, for example, be obtained and used to calculate a cut-off value. *Id.* The cut-off value can then be used, for example, to detect or determine that a subject is affected with RA. *Id.* The specification also provides guidance in Example 1 on page 16 and in Example 4 on pages 17-18 with respect to detecting or differentiating rheumatoid arthritis in RA patients as compared to (1) patients with various other types of arthritis such as gout, pauciarticular arthritis, osteoarthritis, and seronegative spinal arthritis and (2) healthy volunteers. Thus, the specification provides guidance as well as working examples with respect to the claimed subject matter.

Based at least on foregoing, including the guidance provided by the specification, the presence of working examples, and the level of skill for one of ordinary skill in the art in this field, Applicants submit that one of ordinary skill in the art could practice the claimed invention without undue experimentation. In view of the above, Applicants respectfully request reconsideration of the rejection under 35 U.S.C. § 112, first paragraph (enablement) and withdrawal of the same.

**Claim Rejections – 35 U.S.C. § 112, Second Paragraph**

The Office Action rejects claims 1-10 as allegedly indefinite.

In particular, the Office Action rejects claims 1-10 for allegedly lacking a method step tying the measurement of L-PGDS to the preamble, i.e., detecting of differentiating rheumatoid arthritis or determining the degree of dysfunction or determining the stage of disease.

The Office Action also rejects claims 2, 4, and 6, for allegedly setting forth predetermined cut-off values which are “not clear.”

In response, and without acquiescing to the propriety of the rejections, Applicants submit that the instant Amendment is responsive to the present rejections and respectfully request withdrawal of the same.

**Claim Rejections – 35 U.S.C. § 102(a) and (e)**

The Office Action rejects claims 1-10 under 35 U.S.C. § 102(a) as allegedly anticipated by WO 2003/060465 (hereinafter “GUILD”).

The Office Action also rejects claims 1-10 under 35 U.S.C. § 102(e) as allegedly anticipated by GUILD.

Under both rejections, the Office Action alleges that GUILD teaches a method of detecting RA wherein the levels of human L-PGDS in samples collected from a subject are measured. The Office Action further alleges that GUILD teaches determining the stage of RA (“late disease” v. “early disease”) by comparing levels of L-PGDS in those with “late disease” v. “early disease” and that GUILD teaches comparison of the levels of human L-PGDS in RA patients compared to levels in normal patients.

In response, Applicants submit that the claimed subject matter is not anticipated by GUILD. In particular, Applicants submit that GUILD does not teach what the Office asserts. GUILD teaches a list of 490 proteins (“markers”), listed in Table 1, which were identified in the synovial fluid *of patients diagnosed with either erosive or non-erosive RA* (page 85, line 10 – page 86, line 33). Thus, Table 1 is generated from proteins identified only from RA patients; it therefore does not reflect a complete listing of “markers” overexpressed in RA patients *as compared to healthy patients*.

Moreover, Applicants submit that while GUILD pooled serum samples from healthy individuals and compared those to pooled serum samples from patients with RA, these samples were only tested for serum amyloid A (SAA), a marker known to be elevated in RA, and for the presence of “tryptic peptides representing fragments of the endogenous protein calgranulin A, -B, and -C” (page 87, line 17 – page 92, line 32, especially page 91, lines 5-11; see also Table 9B).

With regard to the use of L-PGDS to determine the stage of RA (“late disease” v. “early disease”), Applicants submit that GUILD simply does not teach the use of L-PGDS to determine the stage of RA as the Office asserts. In particular, GUILD appears to disclose very little difference between levels of L-PGDS in patients with erosive and non-erosive RA (see, e.g., marker M177 in Table 1 at page 108).

As stated above, Applicants submit that the cited art does not anticipate the claimed subject matter. However, solely to clarify the record, Applicants further submit that cited art is a WIPO document published July 24, 2003, i.e., more than one year prior to the date of the application for patent in the United States: September 24, 2004. Thus, *if GUILD were*

*anticipatory* it would qualify as art under 102(b) and not 102(a) or 102(e) as set forth in the Office Action.

Based at least on the foregoing, Applicants submit that claims 1-10 are not anticipated by GUILD and respectfully request withdrawal of the rejections under 35 U.S.C. § 102(a) and (e).

### CONCLUSION

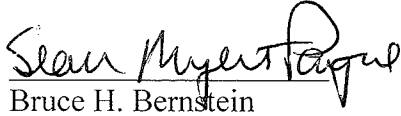
In view of the foregoing remarks, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow each of the pending claims. Applicants therefore respectfully request that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Applicants hereby authorize the U.S. Patent and Trademark Office to charge any required fee to Deposit Account No. 19-0089.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully Submitted,  
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